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ANNUAL REPORT ON
THERMAL AND ELECTRICAL CONDUCTIVITIES
OF BIOLOGICAL FLUIDS AND TISSUES

ONR CONTRACT NO. 4095 (00)

Period

April 1, 1963 to March 31, 1964

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SUMMARY

This report describes Geoscience's research on thermal and electrical conductivities of biological fluids and tissues for the Medicine and Dentistry Branch of the Office of Naval Research (Contract No. 4095 (00)) for the period April 1, 1963 to March 31, 1964.

A literature search on thermal and electrical conductivity of biological fluids and tissues and on the techniques utilized in the cryogenic cooling of biological materials was conducted. Analytical studies have been initiated which will make it possible to estimate or establish the controlling variables of thermal and electrical conductivities of biological fluids and tissue; the results are to be used to correlate more effectively the experimental measurements being obtained.

An existing thermal conductivity apparatus was modified and heat meters and specimen cells for the system were fabricated. Absolute thermal conductivity measurements were obtained for human blood, beef muscle, gastric juice and urine. Conductivity measurements for water were determined with the apparatus during the course of the experiments; the results differed from the literature values by only ±4 per cent. The measurements for blood indicated that the thermal conductivity decreases about 14 per cent as the hematocrit value increases from 0 to 80 per cent. The thermal conductivity of erythrocytes was determined by analysis using a mathematical conduction equation for mixtures. A mean conductivity for the erythrocytes was found to be 0.260 Btu/hr ft°F. Preliminary conductivity measurements were made for beef muscle; the results are compared to some contradictory data found in the literature. Also, some preliminary measurements were made for biological specimens which were slowly frozen and thawed.

The thermal conductivities of human gastric juice and urine were measured and found to be 0.257 and 0.324 Btu/hr ft°F, respectively.

A Sunderman conductivity apparatus was prepared for electrical conductivity measurements of biological fluids. A Wheatstone conductivity bridge and constant temperature bath facility were also constructed. Measurements of whole blood conductivities have been obtained over a 100°F temperature range. The electrical conductivities of human gastric juice and urine were measured as a function of temperature. Electrical conductivity measurements were also made for normal and hemolyzed samples of blood.

For the specific experiments conducted to date, the conductivities of the plasma from the hemolyzed blood were found to be about one half as large as those obtained for plasma from the normal blood.

CONTENTS

I. INTRODUCTION

This research project consists of the determination of the thermal and electrical conductivities of biological fluids and tissues that have been exposed to abnormal physical fields such as temperature and radiation; particular emphasis is given to cryogenic temperature conditions. It is believed that morphological and biochemical alterations in biological fluids and tissues can be detected by measuring resulting changes in thermal and particularly electrical properties. The objective of the program is to establish the relations between changes in the physical properties of biological specimen and the physical stresses imposed upon them.

The thermal conductivities of fluids and tissues are measured using specially constructed apparatus. The electrical conductivities of fluids are determined with commercial equipment; the electrical conductivities of tissues are measured utilizing the cell in the thermal conductivity apparatus. The biological materials being studied are: blood, plasma, cerebrospinal fluid, bone marrow, urine, gastric juice, brain, liver, skin, heart, lung, kidney, stomach, muscle blocks, fatty tissue and tumor tissue. The biological specimens are obtained from animals and humans. Supporting measurements are made to insure the proper biological condition of the specimens; microscopic examinations and biochemical tests are performed and water and lipid contents determined.

The following sections of the report summarize 1) a literature search, 2) analytical and experimental thermal conductivity studies, 3) analytical and experimental electrical conductivity studies, 4) methods for control of biological materials and cryogenic exposure and 5) studies to be conducted during the next year.

II. LITERATURE SURVEY

A literature search has been made on thermal and electrical conductivity measurements for biological fluids and tissues. A survey of rapid cooling techniques in the freezing of biological materials has also been conducted.

The thermal conductivities of some biological fluids have been measured by Spells[1]. Blood, plasma, corpuscles, milk, cream, egg white, egg yolk and cod-liver oil were measured using a comparative method. For the fluids studied, a correlation was found between thermal conductivity and water content. The results of animal tissues reported by other workers were also examined. Other measurements of the thermal conductivity of biological specimens have been reported [2,3]. In these studies, the thermal conductivity constants of such tissues as muscle, lung, brain and liver as well as blood and plasma are given. Also, it is shown that intact muscle and liver conduct better than the homogenized tissues.

A survey has been made of the available data on the temperature dependence of low frequency electrical conductivities of blood, sera, and plasmas. Some of the more important sources[4,5,6,7,8,9,10,11] tabulate the conductivities over the temperature range of 32°F to 130°F. These data have been presented in a graphical form to ascertain most probable, or "normal" values. The resulting charts will be used as a basis of comparison with subsequent experimental data. The literature also disclosed a paucity of data for conductivities of solidified, biological media below 32°F.

A review was made of a number of papers on cryogenic cooling of biological materials. Studies on rapid cooling techniques[12] indicate that cooling rates of specimen can be increased by the application of thin thermally insulating materials; this step shifts cryogenic boiling into the more efficient unstable film or nucleate boiling regime. Thawing is accomplished by immersion in 45°C water. Low-temperature forms of ice have also been studied using X ray diffraction techniques[13,14]; vitreous, cubic and hexagonal phases of ice can exist depending upon cooling rates, additives, and the temperature subsequent to warming. The influence of protective compounds and cooling and warming conditions on hemolysis of erythrocytes by freezing and thawing has also been investigated[15),12]; in general, red cell recovery increases with the concentration of most additives and with an increased freezing rate.

III. THERMAL CONDUCTIVITY STUDIES

A. Theoretical Considerations

Preliminary studies have been initiated to investigate methods for analytically specifying the thermal conductivity of solutions. The thermal conductivity of a solution having no electrostatic field involves the transport of energy by collisions between molecules which essentially vibrate about a mean position within the solution. However, if there is an electrostatic field within the solution (either applied by an outside source or created within the solution by the separation of positive or negative ions because of thermal diffusion etc.) then additional energy will be transported by the flow of ions through the solutions. Analytical thermal conductivity models will make it possible to correlate more effectively the experimental measurements currently being obtained. Further, an analytical relation would help specify the conditions under which conduction would change in biological specimens that have been stressed cryogenically or by other physical fields.

B. Apparatus

The apparatus for measuring the thermal conductivities of biological tissues and fluids was modified and assembled; it consists of a number of components. The heat source is a thin, flat electrical heating element. Heat from this source flows through a thin cell which contains the biological specimens. The cell is composed of two highly conducting plates which contain embedded thermocouples. This feature insures an even heat distribution and thus minimizes free convection. When fluids are being studied, the ends of the plates are sealed by transparent insulating strips which permits the cell contents to be inspected visually. Heat flow through the cell is carried away by an adjacent copper plate which is cooled by a circulating coolant. A thin, flat heat meter which measures the heat flux is located between the conductivity cell and the cooling plate; two of these meters have been fabricated and calibrated. Because of the large width to thickness ratios of these components, one-dimensional heat flow results. Good thermal insulation and guard heating at the edges of the conductivity cell further guarantees one-dimensional heat flow in the system. The heat flux, temperature difference across the sample and sample thickness are measured in this apparatus. The thermal conductivity which is defined as

the heat flux divided by the temperature derivative with respect to distance along the heat flow path is then determined.

Figure 1 shows a cross sectional view of the conductivity cell which is being used to make the property measurements of biological specimens; details of this component are specified in the drawing. Figure 2 shows a photograph of an alternate type of conductivity cell (copper plates with embedded thermocouples and a plastic gasket); a heating element can also be seen in the photograph. Figure 3 shows a photograph of the cooling plate positioned in an insulating container which houses the thermal conductivity cell. Figure 4 shows a photograph of the complete thermal conductivity apparatus; some of its main components are 1) the insulating housing which contains the thermal conductivity cell, 2) the constant head cooling system which supplies cooling water to the cooling plate, 3) the electrical power and metering unit and 4) the potentiometer which is used to measure temperature differences and heat meter voltages.

C. Experimental Results

The thermal conductivity apparatus was used to measure the conductivities of blood, plasma, beef muscle, gastric juice and urine. Prior to these experiments, the heat meters, ammeters and voltmeters used in the apparatus were calibrated. Also, during the period of property measurement of the biological specimens, the thermal conductivity of distilled water was measured numerous times with the apparatus to obtain a continuous check on the accuracy. Typical thermal conductivity measurements for water are shown in Figure 5 together with results published in the literature[16]; note that the water measurements fall within a ±4 per cent scatter band around the established values given in the literature. This agreement is considered to be quite satisfactory; thermal conductivity measurements usually cannot be made as accurately as can electrical conductivity determinations because of such effects as free convection and non-unidirectional heat flow.

Some thirty thermal conductivity measurements of human blood were made using five separate lots of blood from healthy donors. Values were obtained for plasma and high hematocrit samples which were prepared with the aid of laboratory centrifuges. Figure 6 shows a graph of thermal conductivity of blood over a range of hematocrit

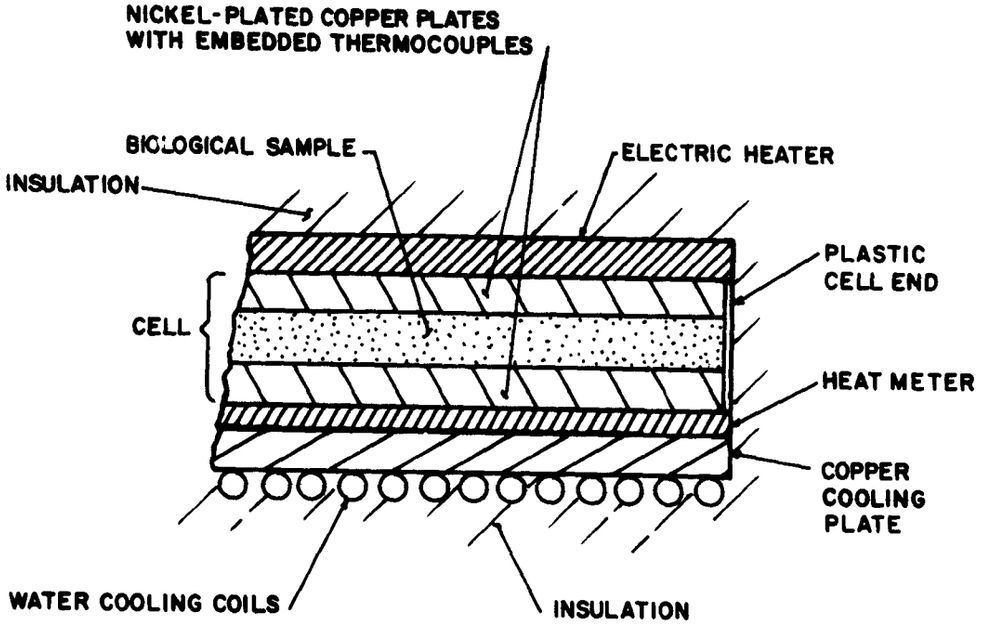

Figure 1. Cross sectional view of thermal conductivity cell.

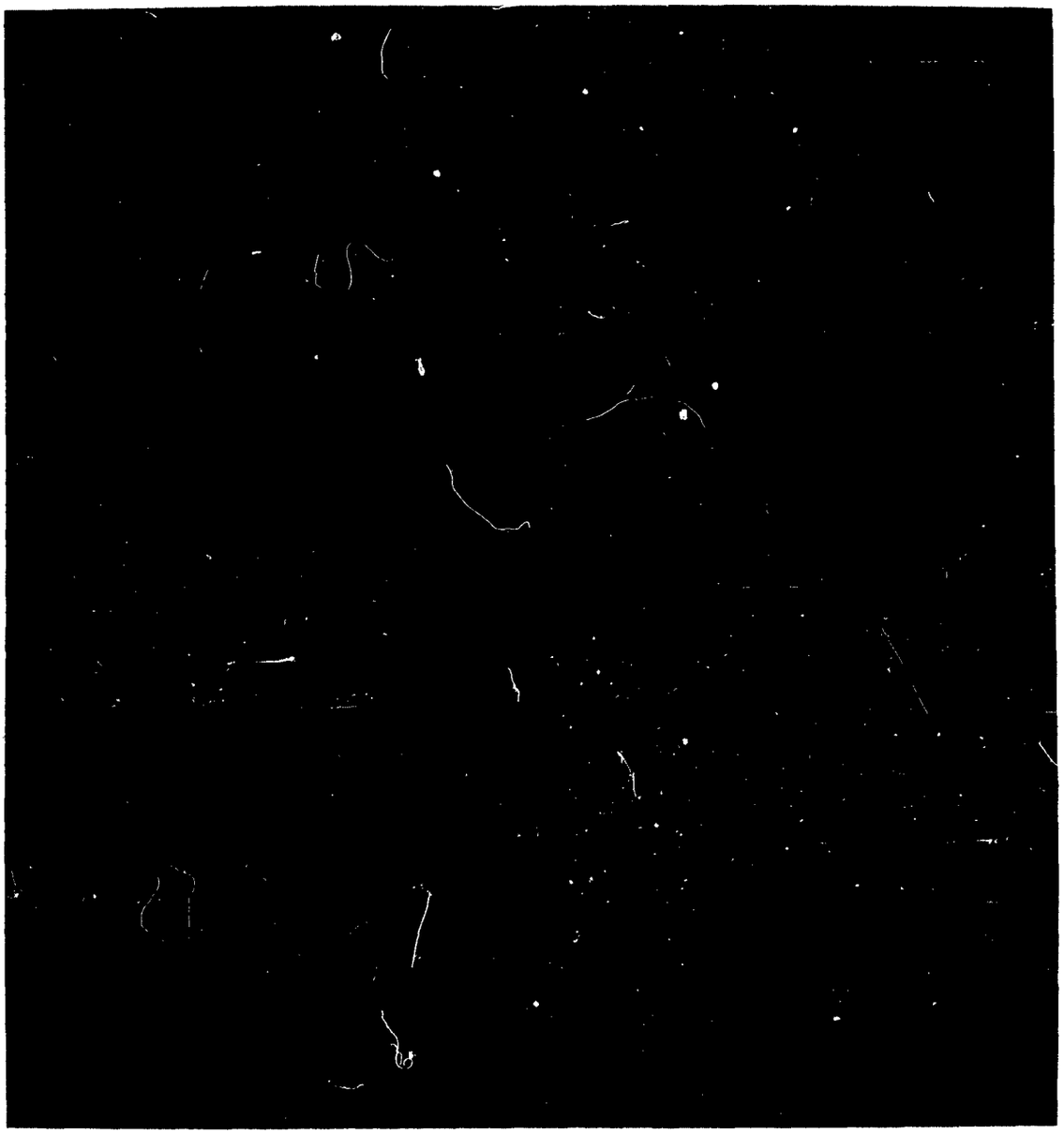

Figure 2. Photograph of a typical, unassembled thermal conductivity cell.

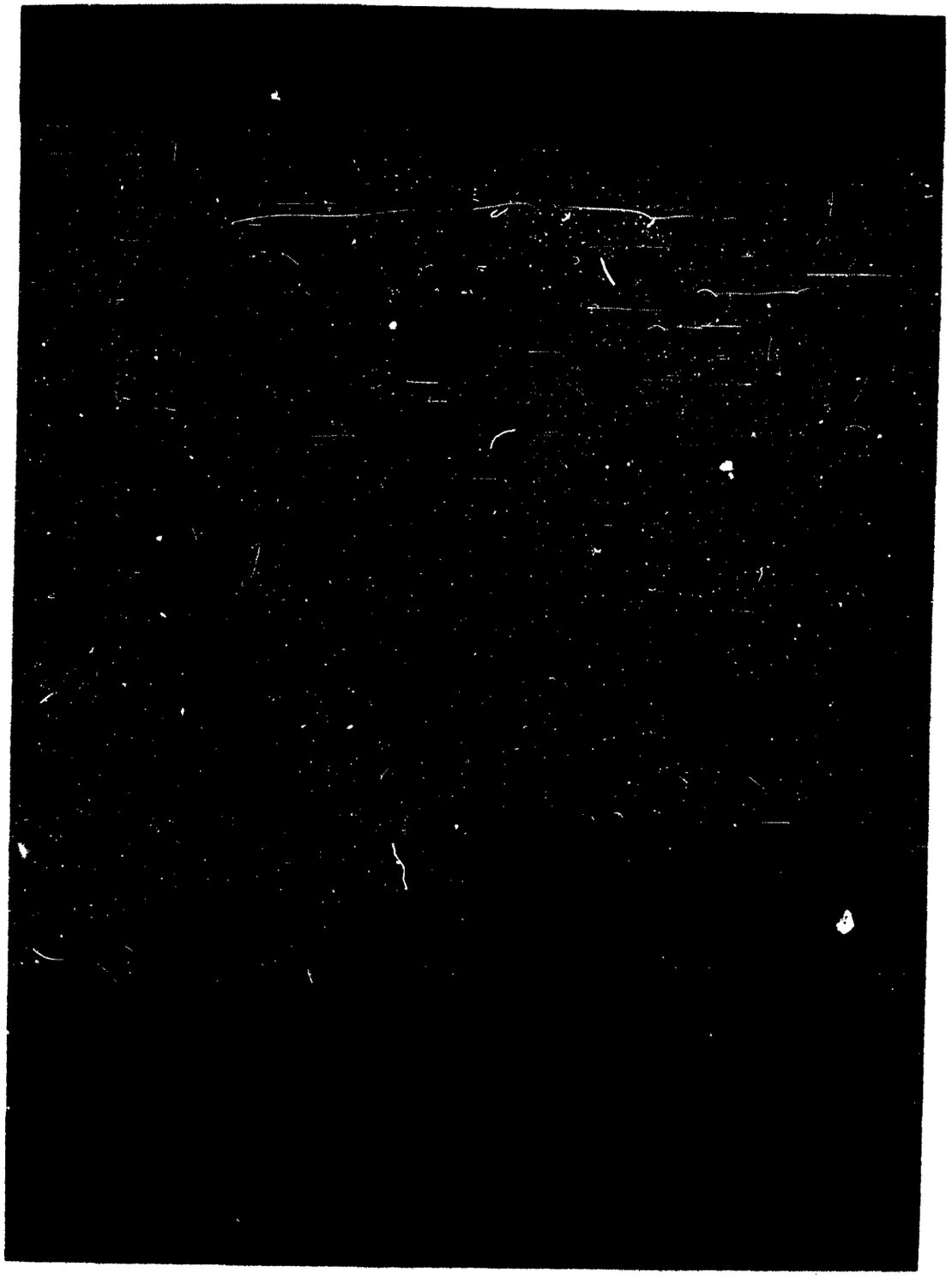

Figure 4. Photograph of the complete thermal conductivity apparatus.

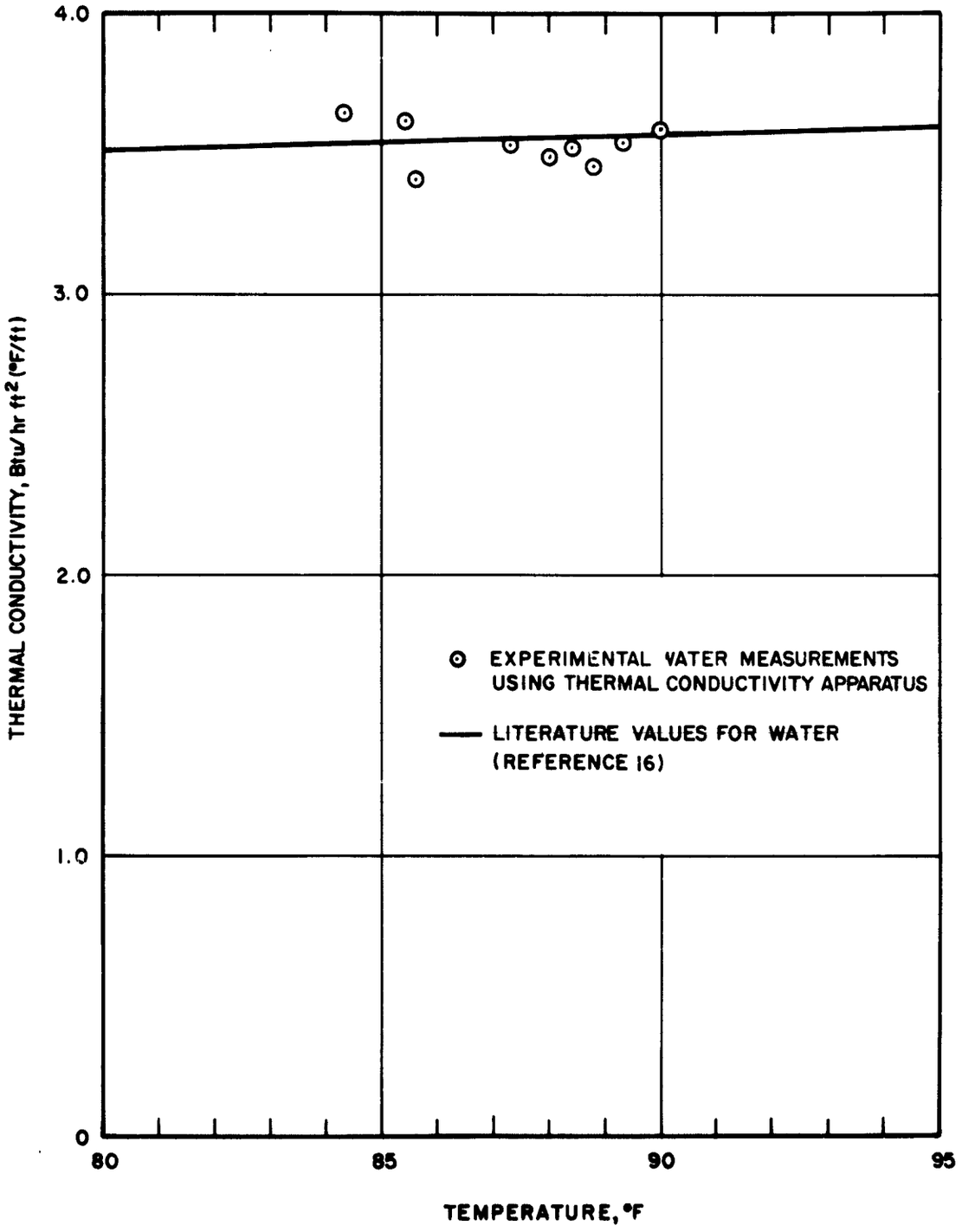

Figure 5. Comparison of typical thermal conductivity measurements for water with literature data.

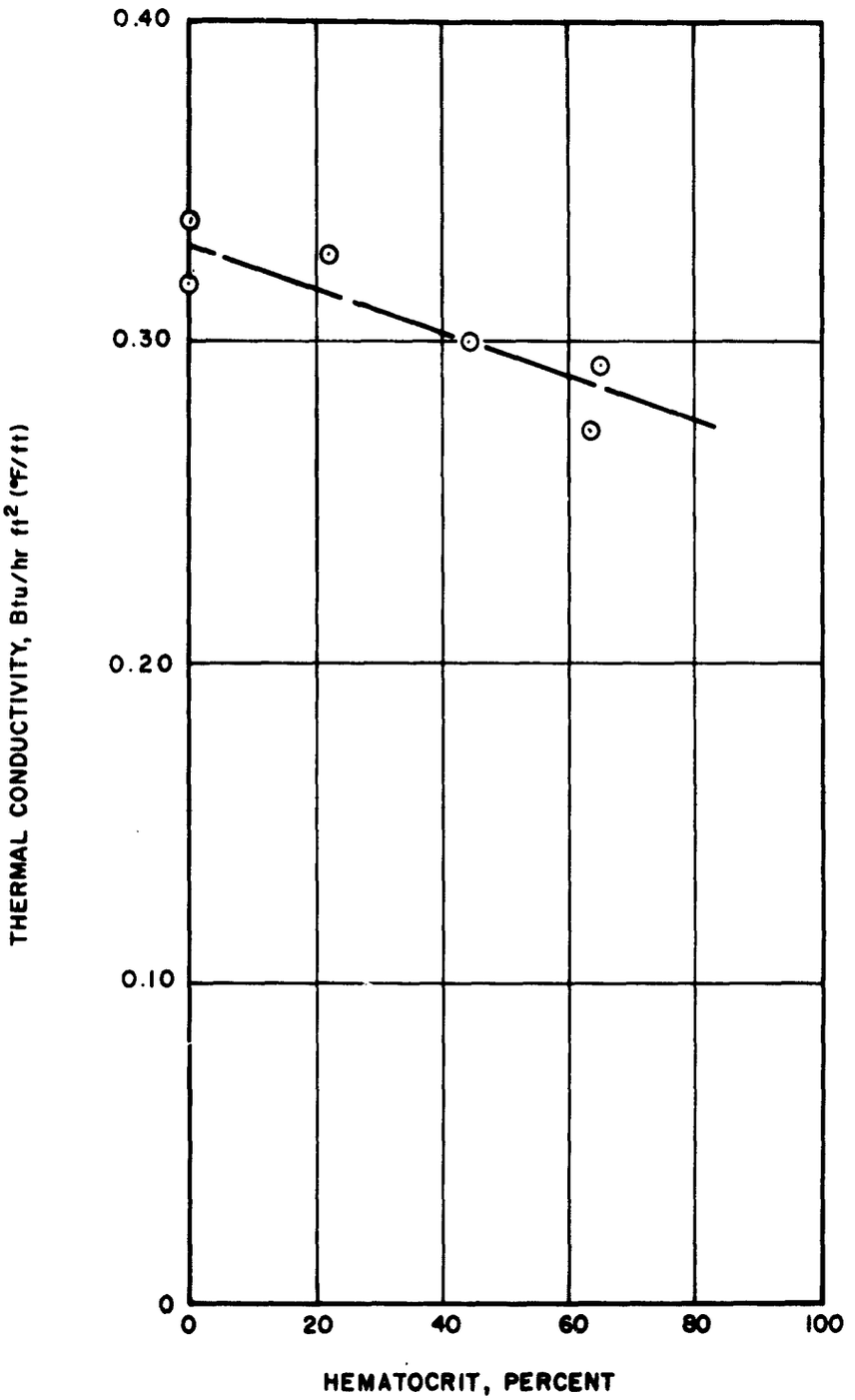

Figure 6. Thermal conductivity measurements of blood as a function of hematocrit ($80 < t < 92°F$).

values*. Note that the conductivity decreases about 14 per cent as the hematocrit value increases from 0 to 80 per cent. Because the blood cells are considered to have better thermal resistance than does the plasma, the curve shown in Figure 6 seems reasonable.

Two thermal conductivity measurements for human blood were found reported in the literature.[17,18] In reference (17), a relative measurement method rather than an absolute method was used to make the determination; a thermal conductivity of 0.293 Btu/hr^2 (°F/ft) was reported. In reference (18), an absolute measurement method was used; a thermal conductivity of 0.39 Btu/hr ft^2 (°F/ft) was reported. From the present study, a value of 0.306 Btu/hr ft^2 (°F/ft) resulted at a normal hematocrit value of about 43 per cent.

During the course of the experiments, attempts were made to find the influence of cell settling on thermal conductivity; none could be detected. This effect is discussed on a theoretical basis in a subsequent paragraph.

The experimental thermal conductivity measurements of blood shown in Figure 6 were analyzed utilizing Eucken's[19] theoretical conductivity equation for uniformly dispersed small particles in a carrier fluid. It is possible to determine the thermal conductivity of the erythrocytes in the blood from the whole blood conductivity measurements by utilizing the Eucken equation†,

$$\frac{k}{k_p} = \frac{1 - \left(1 - a\,\frac{k_c}{k_p}\right) b}{1 + (a-1)\,b} \qquad (1)$$

where, k, conductivity of the mixture (whole blood)

k_p, conductivity of the carrier (plasma)

k_c, conductivity of small particles (erythrocytes)

b, ratio of particle volume to the total volume (the hematocrit value)

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*The thermal conductivities of blood from different donors (for the same hematocrit value and temperature level) were found to differ by as much as six per cent. The experimental points shown in Figure 6 represent mean values for the several lots of blood used.

†Currently other possible conduction models are under investigation.

$$a = \frac{3}{2 + k_c/k_p}$$

Equation (1) can be rearranged to yield an explicit expression for the unknown erythrocyte conductivity, namely,

$$\frac{k_c}{k_p} = \frac{2\frac{k}{k_p} - 2 + 2b + b\frac{k}{k_p}}{2b + b\frac{k}{k_p} - \frac{k}{k_p} + 1} \qquad (2)$$

Upon substituting the experimental conductivity data for whole blood into Equation (2), a mean conductivity for erythrocytes was found to be 0.260 Btu/hr ft°F.

Equation (1) was also used to calculate the influence of the settling of red cells in blood on the thermal conductivity. The results of the study indicated that this effect was small thus verifying the experimental findings.

The thermal conductivities of unstressed human gastric juice and urine were also measured with the conductivity apparatus. The results obtained to date are given in Table 1 together with the previously reported values for human blood and plasma.

Table 1. The thermal conductivity of unstressed biological fluids (75°F < t < 90°F)

Fluid	Thermal Conductivity Btu/hr ft°F
Gastric juice	0.257
Urine	0.324
Blood (hematocrit = 43%)	0.306
Plasma	0.330
Water	0.353

At the time of the literature search on thermal conductivities of biological fluids and tissues, two contradictory values for muscle were tabulated; one value[17] was 0.31 Btu/hr ft^2 (°F/ft) and the other value[18] was 1.33 Btu/hr ft^2 (°F/ft). The latter measurement appeared to be anomalously high for a non-crystalline and non-metallic substance.

Comparisons with other materials and theoretical considerations made the lower value appear to be more reasonable. In this study, thermal conductivity measurements were made on beef muscle in the directions perpendicular and parallel to the grain. A modified version of the thermal conductivity cell shown in Figure 2 was used to make the measurements. A mean value of the conductivity was found to be 0.305 Btu/hr ft^2(°F/ft) which was in good agreement with the conductivity reported in reference (17); the values for heat flow parallel and perpendicular to the muscle grain differed by only a few per cent.

Experiments have been initiated to determine the influence of slow freezing and thawing on changes in the thermal conductivity. Samples of blood and muscle were allowed to freeze to 20°F in a refrigerator and later thaw in a room temperature environment*. To date, only preliminary measurements have been made. The limited results suggest that small changes in the thermal conductivity occur subsequent to the freezing-thawing stress. More experiments must be conducted, however, before definite conclusions can be drawn.

*It is felt that slow freezing and thawing represents an extreme situation in regard to the affect of crystal growth on structural changes in biological specimens.

IV. ELECTRICAL CONDUCTIVITY STUDIES

A. Theoretical Considerations

Most biological fluids contain ions which when acted upon by an electric field will give rise to an electric current within the fluid. The movement or mobility (frequently referred as ionic conductivity) of these ions is influenced by several chemical and physical factors; some factors contributing to an obstruction to the flow of ions while others impel the flow. The chemical complexity of the biological fluids prohibits one from making an accurate theoretical analysis of the electrical conductivity. However, it may be possible to estimate the electrical conductivity if one is familiar with the principle factors involved in the calculation. Once these factors are known it is then essential to relate them to the morphological and biochemical structure of the biological fluids.

A discussion of the more successful theories of electrical conductivity and of the principle factors involved is presented in the following paragraphs. The more useful quantity, the equivalent conductivity, Λ, is utilized. The equivalent conductivity is relative to the more familiar specific conductivity, K_{sp}, by Equation (3).

$$\Lambda = 1000 \frac{K_{sp}}{C} , \tag{3}$$

where, Λ = equivalent conductivity, $cm^2\ ohm^{-1}\ gram\text{-}equivalent^{-1}$,

K_{sp} = specific conductivity, $ohm^{-1}\ cm^{-1}$,

C = concentration, gram-equivalent/liter solution (normality).

The theory of electrical conductivity is very successful for very dilute solutions containing uni-univalent electrolytes that completely dissociate in solution (e.g., NaCl). The equation for the electrical conductivity of these very dilute solutions is know as the Onsager limiting law and is valid for concentrations less than 0.001 N (Onsager's limiting law gives an 8 per cent error in Λ for a 0.1 N aqueous NaCl solution at 25°C). Onsager's limiting law[20] for uni-univalent electrolytes becomes:

$$\Lambda = \Lambda^\circ - \left[\frac{8.204 \times 10^5\ \Lambda^\circ}{(\epsilon T)^{3/2}} + \frac{82.5}{\eta(\epsilon T)^{1/2}} \right] \sqrt{C} , \tag{4}$$

where, Λ = equivalent conductivity, $cm^2\ ohm^{-1}\ gram\text{-}equivalent^{-1}$,

Λ° = equivalent conductivity at zero concentration,

ϵ = dielectric constant of solvent,

η = viscosity of solvent, poise,

T = temperature, °K,

C = normality, gram-equivalent/liter solution.

The limiting equivalent conductivity Λ° is the sum of the limiting ionic equivalent conductivities λ° of the ions in solution. Thus for an electrolyte giving two kinds of ions:

$$\Lambda^\circ = \lambda^\circ_1, + \lambda^\circ_2 \ . \tag{5}$$

The limiting ionic conductivities are primarily a function of their ionic radius (including hydration) and the viscosity of the solvent. In an aqueous solution the ionic conductivities will increase by a factor of 5 to 6 over the range 0° to 100°C. This increase is closely related to the decreasing viscosity of the water; it can be shown that the product $\lambda^\circ\eta^\circ$ (η° = the viscosity of water) is a constant for large ions (total ionic radius greater than 5 Å) over the range 0° to 100° and that this product for smaller ions varies by only 30 per cent at most between these limits. For fixed temperature, λ° will decrease with an increase in the viscosity of the solution; the increase in η may be brought about by the addition of a neutral material to the solvent (e.g. sucrose). Onsager's limiting law states that at a given temperature the equivalent conductivity decreases with increasing concentration (the specific conductivity increases) which is experimentally verified for those electrolytes which completely dissociate.

For higher concentrations Robinson and Stokes[21] modified Equation (4) to allow for the finite size of the ions. Their equation for an uni-univalent electrolyte is:

$$\Lambda = \Lambda^\circ - \left[\frac{8.204 \times 10^5\ \Lambda^\circ}{(\epsilon T)^{3/2}} + \frac{82.5}{\eta(\epsilon T)^{1/2}}\right] \frac{\sqrt{C}}{\left[1 + \frac{50.29 \times 10^8\ \dot{a}\sqrt{C}}{(\epsilon T)^{1/2}}\right]}, \tag{6}$$

where $\dot{a}$ is the ion-size parameter in centimeters and all other quantities are the same as given in Equation (4). The ion-size parameter which can be expected to lie in the range 3-5.5 Å for most simple ions has been found to be nearly independent of temperature for fully dissociated 1:1 electrolytes. Equation (6) will accurately represent Λ for an aqueous

NaCl solution to 0.1 N when a value of 4 Å is used for å (Equation (6) gives a 2.3 per cent error for a 1.0 N aqueous NaCl solution at 25°C).

The viscosities used in Equations (4) and (6) are those for a pure solvent. An improvement may result in predicting Λ if the actual viscosity of the solution is used. For very dilute solutions where Equation (4) is valid, this improvement is not significant, however, for more concentrated solutions use of the actual viscosity of the solution extends the range of Equation (6) to higher concentrations.

Models used to calculate the relative viscosity (compared to water at the same temperature) of a solution have been derived by Falkenhagen et al., and by Einstein. For very dilute solutions containing small ions, Falkenhagen's limiting law[22] gives:

$$\eta_{rel} = 1 + A_1\sqrt{C}\ , \tag{7}$$

where, $\eta_{rel} = \eta_{solution} / \eta_{water}$,

A_1 = 0.005 to 0.03 mole$^{-1/2}$ liter$^{1/2}$, depending upon electrolyte,

C = molar concentration, mole/liter solution.

Equation (7) is valid to concentrations of 0.001 N. For more concentrated solutions Jones and Dole[23] extend Equation (7) to give the empirical equation:

$$\eta_{rel} = 1 + A_1\sqrt{C} + A_2 C, \tag{8}$$

where A_2 is an empirical constant which can be negative or positive. For large spherical molecules (e.g., colloids) Einstein's equation[24] for dilute solutions gives:

$$\eta_{rel} = 1 + 2.5\ \phi\ , \tag{9}$$

where ϕ is the volume-fraction of the solute molecules. For higher concentrations Equation (9) is modified to give:

$$\log \eta_{rel} = \frac{A_3 C}{1 - Q'C}\ , \tag{10}$$

where, $A_3 = 2.5\ \bar{V} / 2.303$,

$\bar{V}$ = effective rigid molar volume of solute, liter/mole,

$Q' = Q\ \bar{V}$

Q = empirical constant that is approximately unity,

C = molar concentration, mole/liter solution.

Equation (10) may be used to represent the relative viscosity of some solutions up to values ten times that of water.

The conductivity of a solution decreases at fixed temperature with an increase in the viscosity of the solution. However, for small ions (total ionic radii less than 5 Å) the decrease in Λ is not directly proportional to the fluidity of the solution (the product $\Lambda\eta$ is not a constant). For example, the limiting conductance Λ° of KCl in sucrose solutions obeys the empirical relation $\Lambda^\circ \eta^{0.7}$ = constant. Thus for 20 per cent sucrose solution of relative viscosity 1.9 at 25°C, the limiting conductance of KCl is reduced to 0.629 of that in pure water.

Another factor which reduces the conductance of a solution is the incomplete dissociation of the electrolyte. There has been no evidence of ion-pairs in aqueous solutions of NaCl or KCl, however, the phosphates, sulphates, nitrates etc. of these cations have been found to associate in solution. At infinite dilution these electrolytes will be completely dissociated and each ion will contribute to the conductance of the solution. However, at higher concentrations a fraction of the electrolyte will be associated as neutral molecules thus decreasing the conductance from what it would be if there was complete dissociation.

A mixture of electrolytes with dissimilar ionic conductivities (e.g., the biological fluids) will have an equivalent conductance which is different than that calculated assuming the additive laws. For electrolytes with similar ionic conductivities, the additive laws are valid to concentrations of 1.0 N. Binary and ternary mixtures of NaCl, KCl and HCl may be represented by the additive laws to within one per cent at 1.0 N total concentration.

The additive laws that seem to hold for mixtures are the following: For the relative viscosity,

$$\eta = \sum X_i \eta_i, \tag{11}$$

where, η = relative viscosity of mixture at total electrolyte concentration C,

η_i = relative viscosity of solutions of pure salts of concentration C,

X_i = mole fraction of the ions.

For the equivalent conductivity of mistures,

$$\Lambda = \sum X_i \Lambda_i, \tag{12}$$

where, Λ = equivalent conductivity of mixture at total electrolyte concentration C,

Λ_i = equivalent conductivity of the pure salts in solution at a concentration C,

X_i = mole fraction of the ions.

The above discussion has been a review of the principle factors involved in calculating the electrical conductivity of simple electrolytic solutions. A theory for the electrical conductivity of concentrated, chemically complex solutions has not been developed. Although most biological fluids are chemically complex their electrolyte concentration is moderately low, therefore, it is hoped that present day theories may be applied to these fluids. First, however, a complete understanding of the chemical nature of these fluids is required; not only are the chemical compositions required but also estimates of possible chemical changes of the constituents when these biological fluids are subjected to various physical processes (e.g., freezing, heating, fluid shear stress, passage of electric current etc.).

B. Apparatus

A Sunderman direct-reading conductivity bridge for biological fluids with an appropriate cell has been used to measure the electrical conduction of biological fluids. The bridge is capable of making measurements at both 60 cycles/sec and 1000 cycles/sec to discern the effects of polarization at the electrode surfaces. The following major items of apparatus were utilized in the electrical conductivity measurements:

1. Signal generator, EICO, Model 377.
2. Decade resistor, variable, precision, 0 - 2000 ohms.
3. Decade capacitor, variable, precision, 0 - 1 μfd, 100 $\mu\mu$fd steps.
4. Both temperature controller Porta-Temp, P.S. Co., range: $\pm$ 0.25°C, $\pm$ 0.125°C sensitivity.
5. Oscilloscope, Tektronix, type 504.
6. Thermometer, precision, $\pm$ 0.01°C.
7. Bridge, conductivity, Sunderman.
8. Cell, conductivity, Sunderman, nominal constant: 10.6 per cm.
9. Solutions, conductivity, KCl, NaCl (standards).

Electrical resistance is the resistance to the flow of electrons in a solid, or the movement of ions in a liquid, and is likewise dependent on the nature of the particular substance, dimensions, and temperature. From Ohm's law, the resistance to the passage of a current through a conductor of uniform cross-section may be represented by

$$R = \rho \frac{L}{A} = \frac{L}{\sigma A} \tag{13}$$

where, R is resistance in ohms; ρ, resistivity, ohm-cm; L, length, cm; A, cross section, cm^2; σ, conductivity, $(ohm\text{-}cm)^{-1}$.

In a conductivity cell, the dimensions of the liquid sample are constant, hence, Equation (1) may be defined in terms of a constant, C, as follows:

$$C = \sigma R \tag{14}$$

The constant, C, may be either calculated from the dimensions of the cell, or calibrated by means of a solution whose conductivity is precisely known. The resistance, R, is measured with a modified Wheatstone bridge powered by a high frequency source (1000 cycles per sec.).

Because electrolytic solutions possess inherent capacities, an electrical source impressed across an electrolyte develops a current which is out of phase with the voltage. The desired resistance component may, however, be derived from a knowledge of the amount of parallel capacitance required in the opposing arm of the Wheatstone bridge to achieve balance. From electrical theory it can be shown that

$$\tan \alpha = 2\pi f C R_{measured} \tag{15}$$

where, α is the phase angle, radians; f, frequency, cps; C, capacitance, farads; R, measured resistance, ohms.

The resistive component of the total electrolyte impedance can be obtained from the measured value and the phase angle:

$$R = R_{measured} \cos^2 \alpha \qquad (16)$$

The Sunderman conductivity cell used for the electrical conductivity measurements reported in this study was stated by the manufacturer to possess a constant of 10.6 per cm. This value was verified by means of two standard NaCl and KCl solutions. Resistance measurements with both solutions at a fixed temperature yielded an initial cell constant of 10.69 per cm. Throughout the subsequent series of blood conductivity measurements, the cell constant increased to a value of 10.90 per cm.

C. Experimental Results

The values for the electrical conductivity of human blood and sera from the literature are presented in Figure 7 as a function of temperature. The ranges indicated in the above figure encompass 95% of the available conductivity values. Also presented in Figure 7 are the results of approximately 150 separate determinations of whole blood conductivities; these data fall within a band which includes 95% of the experimental values. In all series of experiments, a small amount of heparin was used to prevent coagulation. It is estimated that the experimental values are accurate within ± 2%. These data were studied in order to establish the precision with which the conductivities of various samples can be determined.

Figure 8 illustrates the sensitivity of electrical conductivity as a means for determining small variations in the distribution of the physical constituents of whole blood with time. These measurements were made with the apparatus described previously. The average deviations for both sets of data having the indicated hematocrit values were ±1%. The rate of change of electrical conductivity or settling was found to be strongly dependent on the position of the conductivity cell with respect to the earth's gravitational field. The results shown in Figure 8 indicate that measurements must be obtained immediately after a uniformly dispersed sample is placed in the conductivity cell.

In Figure 9, the electrical conductivity measurements of whole human blood are presented as a function of temperature with various hematocrit values as parameters. The precision of these sets of experimental data was such that the maximum deviation was not greater than ±1% from the given curves.

The electrical conductivities of human urine and gastric juice were measured as a function of temperature in a controlled temperature bath to about 80°C. The resulting

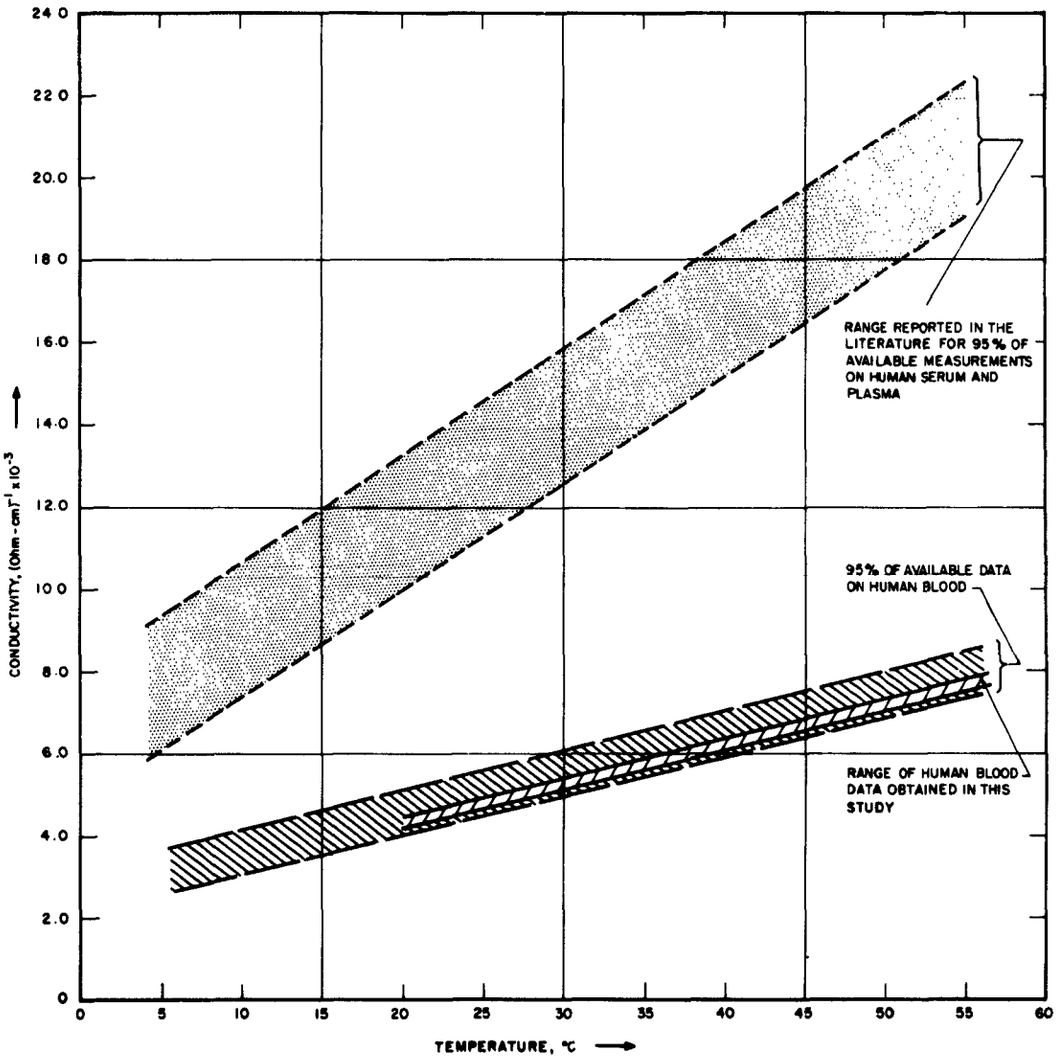

Figure 7 Electrical conductivity variation of human blood, plasma and sera with temperature.

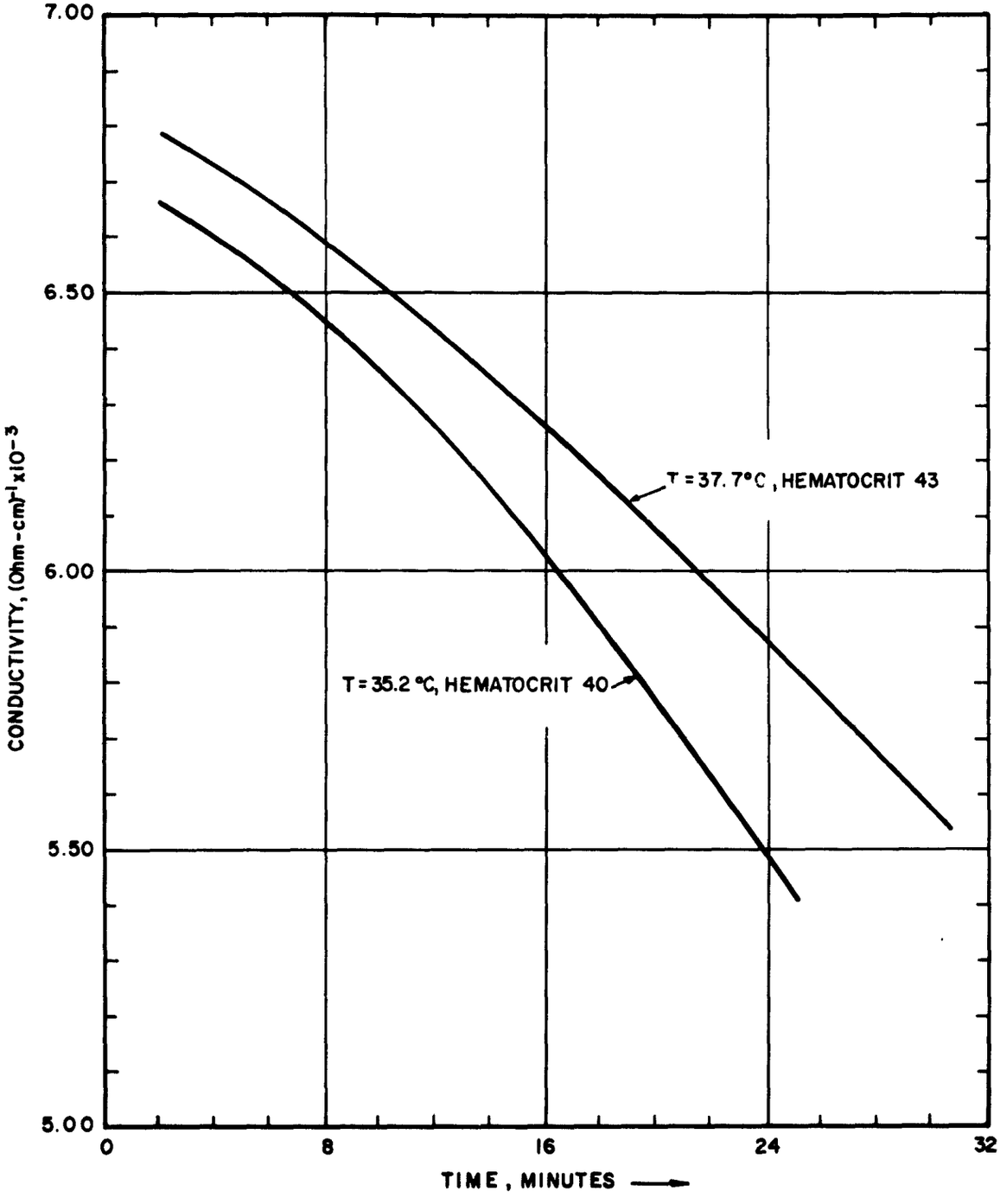

Figure 8. Variation of electrical conductivity in quiescent human blood with time.

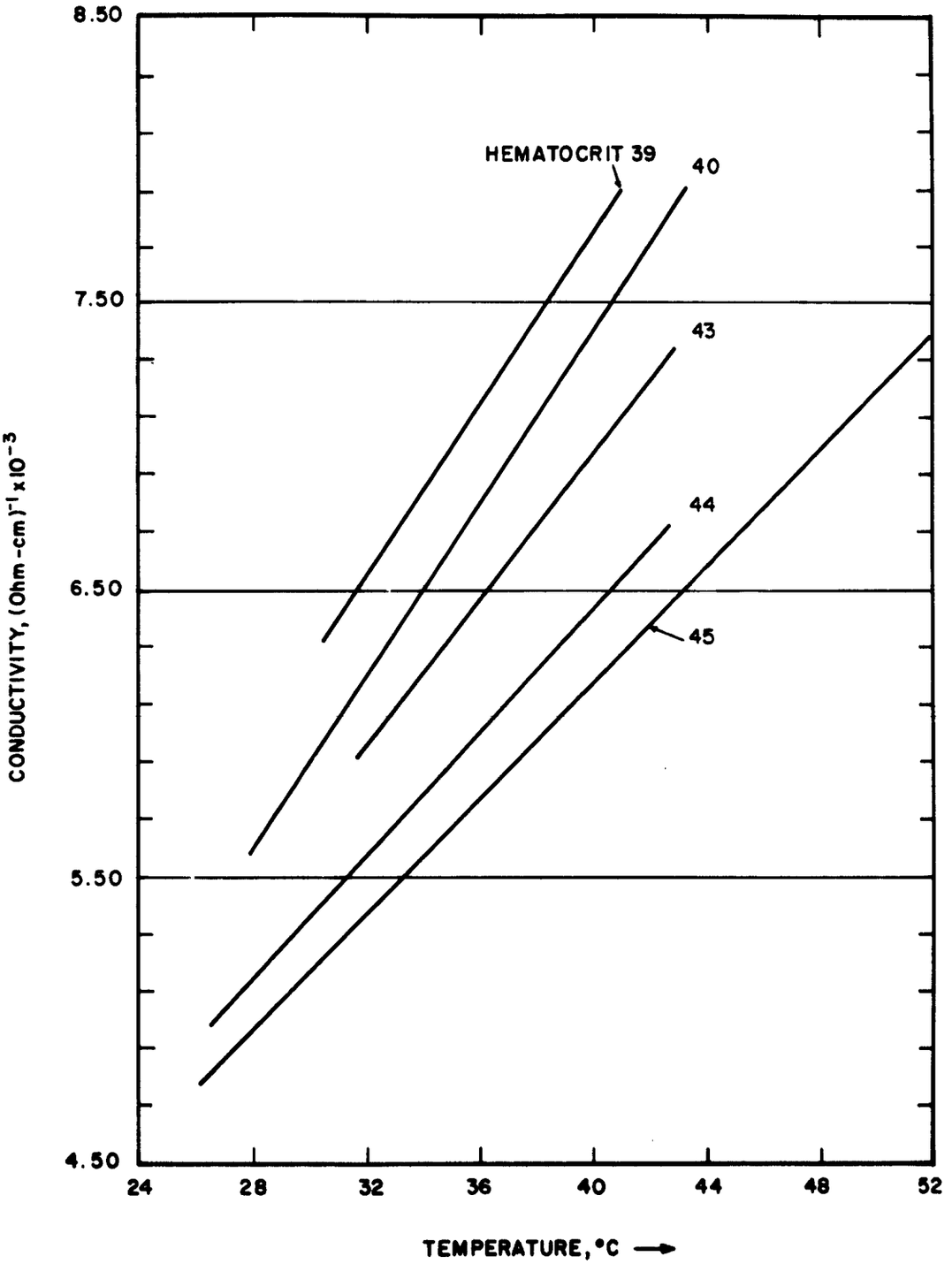

Figure 9. Electrical conductivity variation of human blood with various hematocrit values.

conductivity distribution with temperature for urine is shown in Figure 10. Twenty-four hours following this series of measurements, room temperature conductivities of the same sample were redetermined with the results as indicated in Figure 10. Human gastric juice conductivities of samples obtained from the U. S. Naval Hospital in San Diego were also determined with the conductivity apparatus. The procedure used to make these measurements was identical with that employed in the urine measurements. Two complete sets of data were obtained on alternate days to determine the effects of heating on this nearly pure ionic solution. The results of these measurements are shown in Figure 11, where, within the accuracies of the equipment, no discernible dispersion between the two sets of data is evident.

Because the fraction of colloidal matter in both urine and gastric juices is relatively small, no irreversible change would be expected with temperature in these simple ionic fluids. The data obtained during these measurements would seem to verify such a hypothesis. Blood, however, would not be expected to exhibit similar reversible properties when the temperature level exceeds that value at which thermal hemolysis becomes of importance. Preliminary measurements of blood conductivity at higher temperatures indicate the existence of an irreversible change.

Initial determinations of electrical conductivities of hemolyzed and non-hemolyzed blood were made using whole blood; subsequent experiments were conducted with plasma that had been separated from the whole blood to eliminate the variable introduced by erythrocyte settling. The results of these initial experiments can be seen in Figure 12. Note that the conductivity increases markedly from 50°C to 65°C. This large change in conductivity is an excellent index of morphological and biochemical changes in this specimen.

To nullify the effects of erythrocyte settling on electrical conductivity, the liquid phase constituent was separated from the hemolyzed blood. A standard centrifuge technique was used to separate the plasma from the platelets by exposure to 800 gravities for ten minutes. The electrical conductivities of the plasma, which contain the products of varying degrees of hemolysis, were measured as a function of temperature. The results of these preliminary control measurements are presented graphically in Figure 13 where, it may be noted, a factor of about two exists between the conductivities of normal and severely hemolyzed blood plasma. Conductivity data for a 50% dilution of the severely hemolyzed sample were found to fall as predicted between the severely hemolyzed plasma and the plasma from

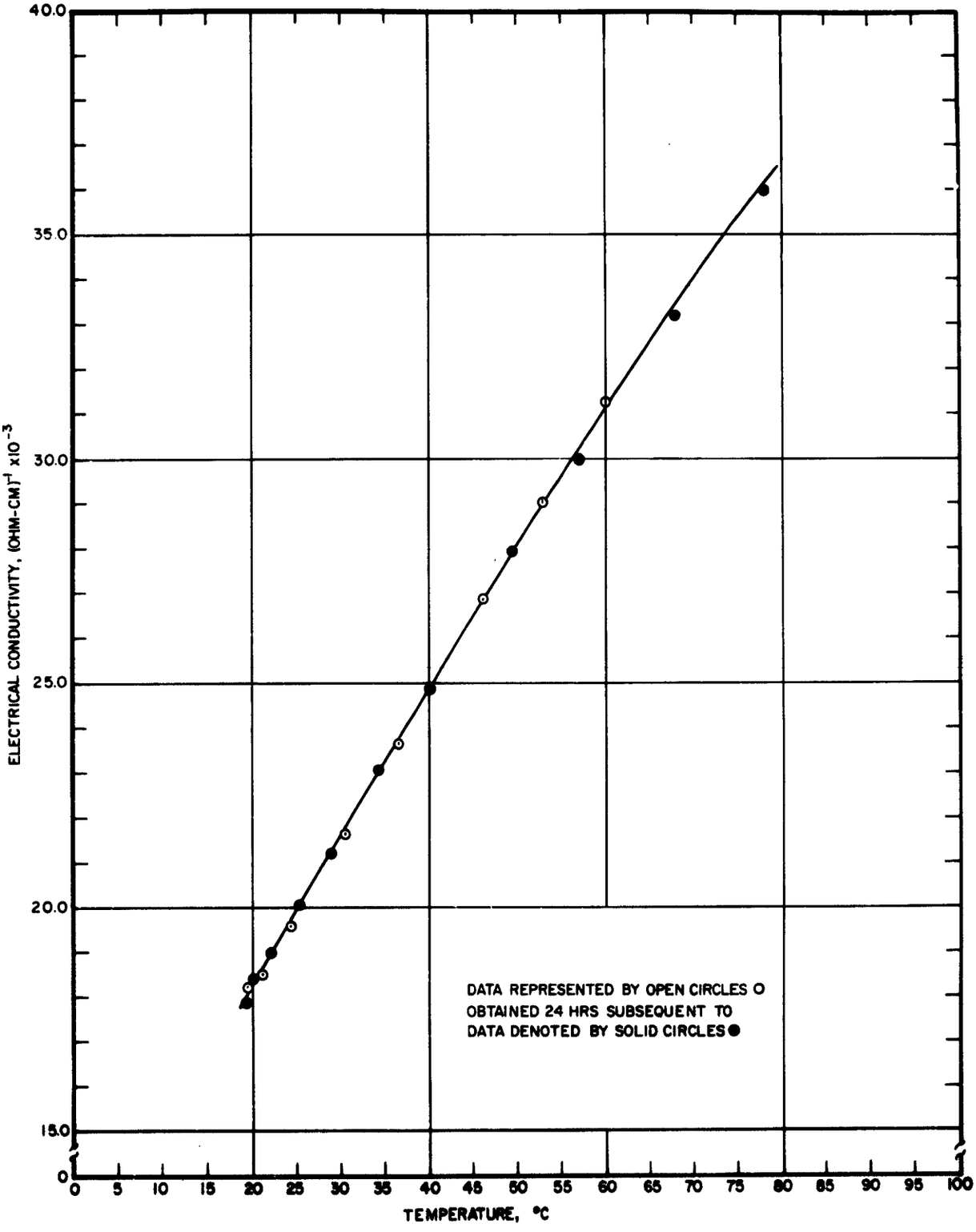

Figure 10. Electrical conductivity of human urine sample.

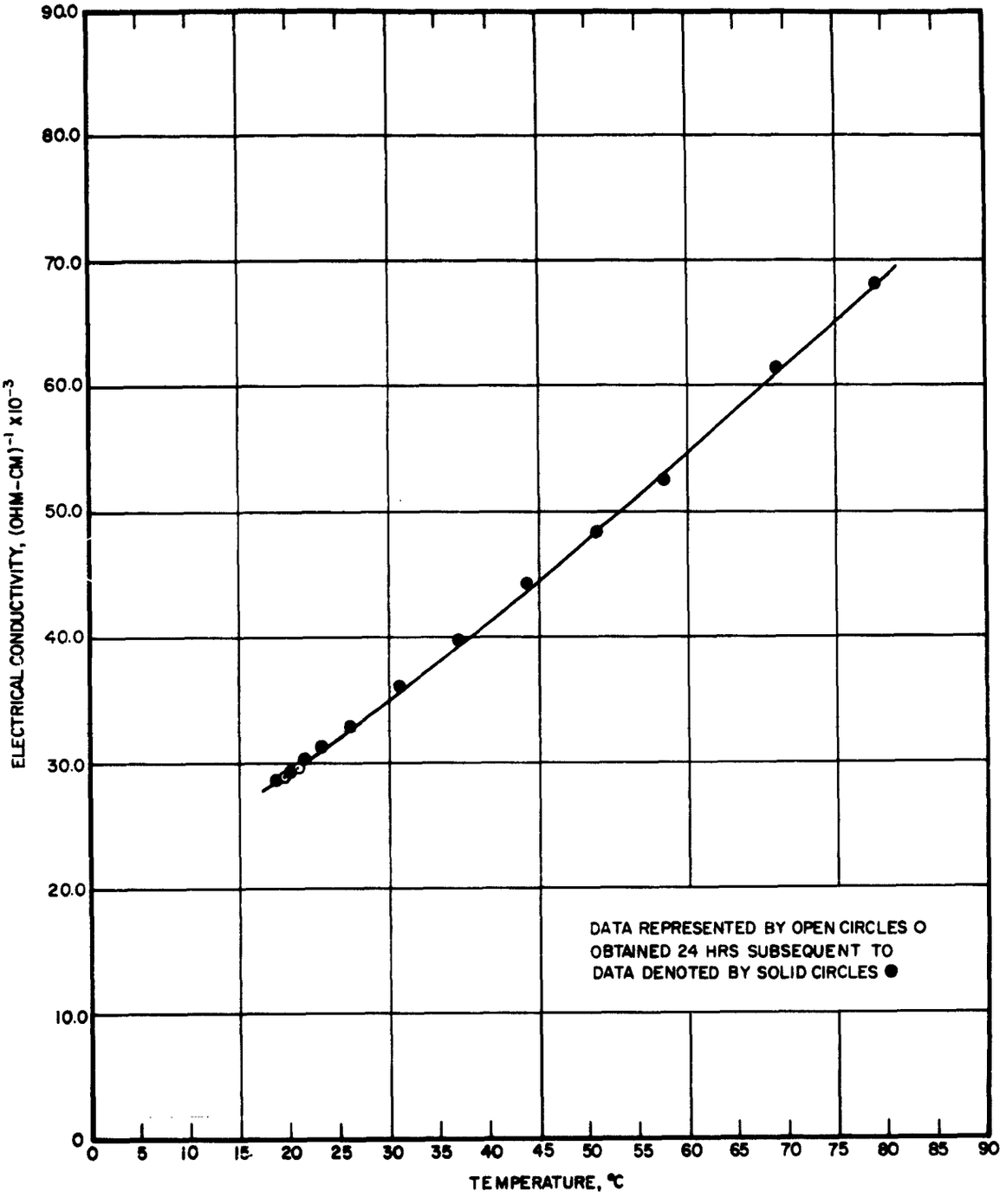

Figure 11. Electrical conductivity of human gastric juice.

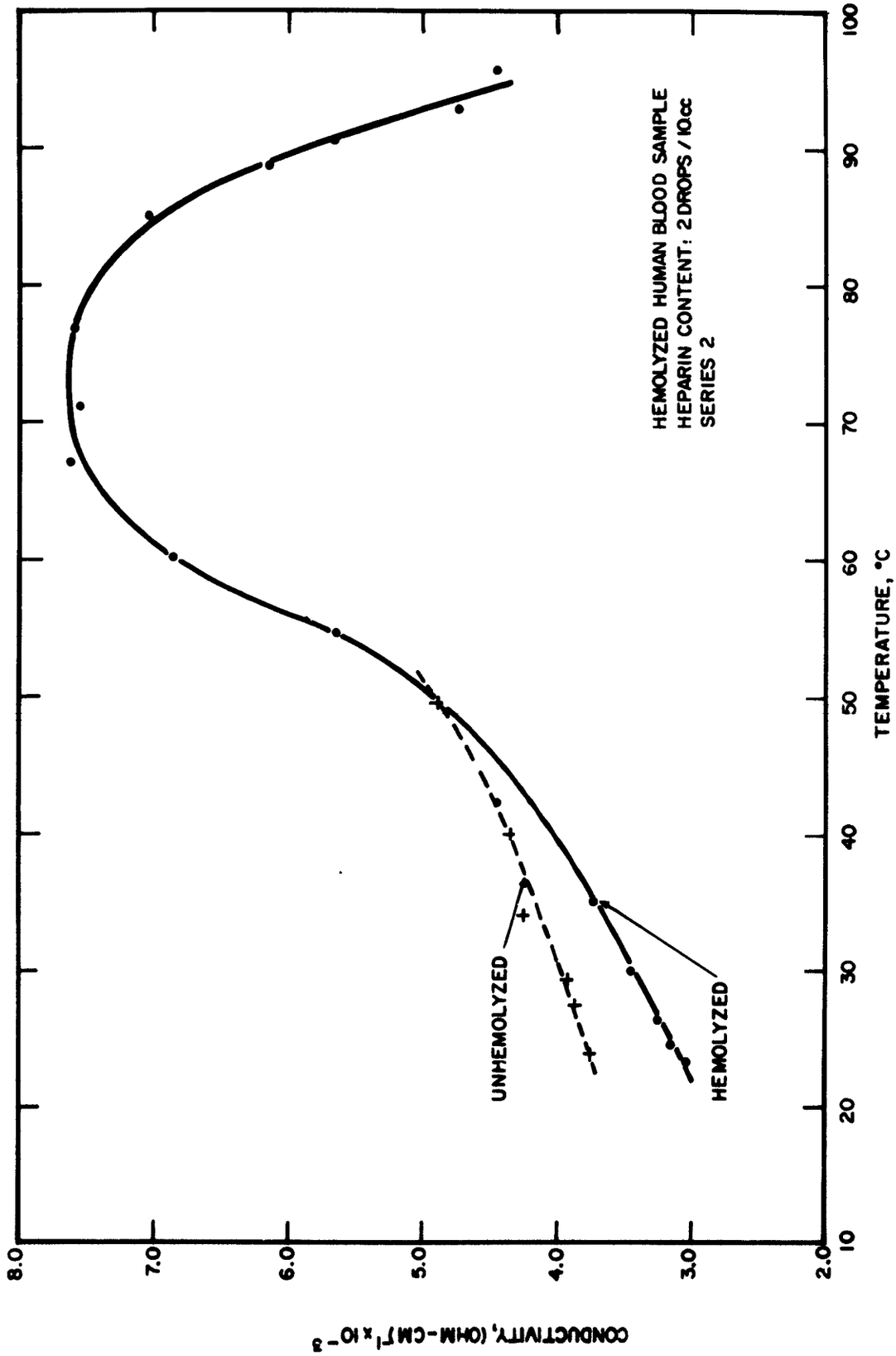

Figure 12. Electrical conductivity of hemolyzed blood with temperature.

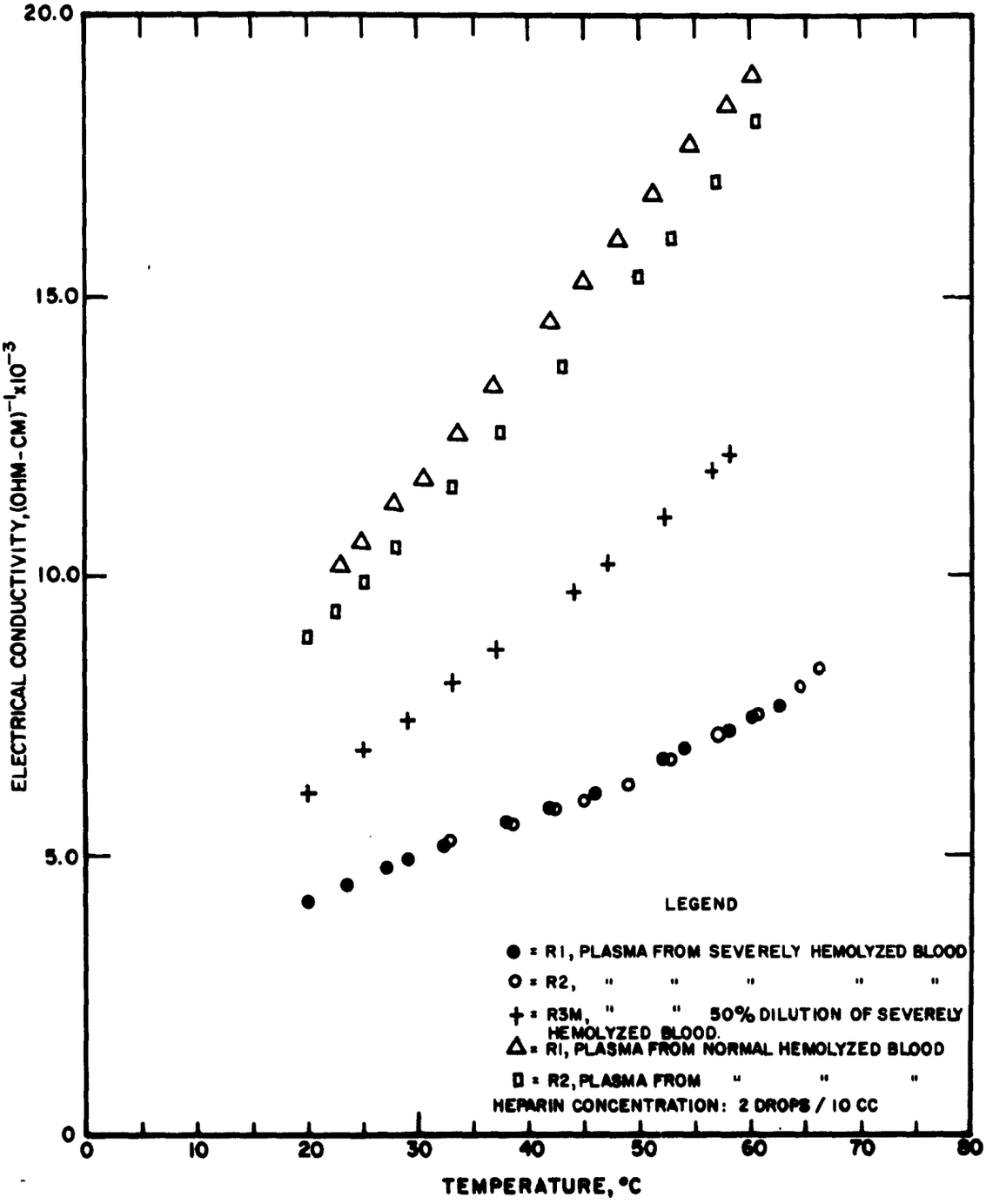

Figure 13. Electrical conductivity of hemolyzed human blood plasma with temperature.

normal blood. The differences between the conductivities of the two minimum hemolysis samples is attributed to a small difference in hemolysis which was not detectible by the existing method for hemolysis determination. The large differences between the electrical conductivities of hemolyzed and non-hemolyzed plasma, and the excellent repeatability of the data would seem to propose a sensitive criterion or test for all degrees of blood damage or hemolysis and probably other morphological and biochemical changes in biological fluids.

V. CONTROL OF BIOLOGICAL MATERIAL AND BIOLOGICAL EXPOSURE

Biological specimens are and will be obtained from healthy animals including rats, mice, cats, dogs and cattle; all samples will be taken surgically under sterile conditions. Some human blood samples are also used. Confirmation of tissue structure and ultra-structure will be obtained with the aid of optical and electron microscopes when required. The samples are fixed by immersion in buffered formalin prior to pathological analyses. Standard biochemical checks on the biological fluids are and will also be made including hemolysis measurements for blood.

Cryogenic storage and freezing containers for blood and tissue samples are being acquired through the Air Reduction Corporation in preparation for property measurement of specimens that have been exposed to rapid freezing and thawing.

VI. STUDIES TO BE CONDUCTED DURING THE NEXT YEAR

During the next year it is proposed to investigate the following biological specimens:

Specimens	Source
Fluids	
Spinal (human cadaver or specimen)	U. S. Naval Hospital*
Semen (beef, ram)	Naval Medical Research Institute*
Marrow (horse abattoir)	San Diego Zoo
Serum (human)	Geoscience
Blood† (human)	Geoscience
Gastric juice (human, autopsy)	U. S. Naval Hospital
Aqueous humor (human, autopsy)	U. S. Naval Hospital
Tears	Geoscience
Urine	Geoscience
Tissues	
Skin (human epidermis and dermis, autopsy)	U. S. Naval Hospital
Brain (human, autopsy)	U. S. Naval Hospital
Liver (animal, human)	U. S. Naval Hospital, Zoo
Lung (animal, human)	U. S. Naval Hospital, Zoo
Kidney (animal, human)	U. S. Naval Hospital, Zoo
Cornea (animal, human)	U. S. Naval Hospital, Zoo
Bone (horse abattoir)	San Diego Zoo

*Arrangements have been made with staff members of the U. S. Naval Hospital in San Diego and the Naval Medical Research Institute in Bethesda, Maryland, for the procurement of the indicated specimens.

†Only long term property changes would be studied because most of the blood investigations will have been completed during Phase 1.

A staff member of the Naval Medical Research Institute has made cryogenic depository facilities available to Geoscience. Specimens will be frozen and stored at NMRI until required for property measurements. The specimens will then be shipped to Geoscience where thawing will be accomplished prior to property analyses. Some cryogenic studies, of course, will not require the use of the NMRI storage facilities; many specimens will be frozen and thawed at Geoscience prior to study.

Some thermal and electrical conductivity measurements of biological specimens will also be conducted at temperatures greater than body temperature. Geoscience studies have already shown unusual, permanent increases in the electrical conductivity of plasma when exposed to temperatures in excess of about 140°F. An effort will be made to establish further the temperature levels at which such changes occur.

The experimental thermal and electrical conductivities of the biological specimens will be correlated with imposed temperature stresses and morphological and biochemical alterations.

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